IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Emerging Biomarkers In Cancer, Diabetes, And Kidney Stone Disease: Diagnostic And Therapeutic Insights

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Abstract:-

Measurable signs known as biomarkers are used to diagnose illnesses, track their development, and assess the efficacy of therapies. Important biomarkers for kidney stone disease, diabetes, and cancer—three major global health issues—are covered in this review. Circular RNAs, survivin, protein markers, circulating tumour DNA, and exosomes are examples of biomarkers in cancer that help in early identification, outcome prediction, and targeted therapy guidance. Serum indicators, cardiac markers, HbA1c, circular microRNAs, and glycated albumin are examples of diabetes biomarkers that can evaluate glucose control, identify problems early, and enhance diagnosis. Calcium oxalate-binding proteins and metabolic markers are examples of kidney stone biomarkers that help in early stone risk assessment and improved recurrence treatment. These biomarkers are crucial instruments for contemporary clinical practice since they enhance diagnosis, tracking, and individualised treatment.

Keywords :–

Biomarkers,Precision medicine , Cancer biomarkers ,Diabetes biomarkers ,Kidney stone disease HbA1c ,microRNA

Introduction :-

The definition of a biomarker is surprisingly straightforward: "A measurable attribute that is used to assess pathogenic processes, normal biological processes, or reactions to exposure or intervention." This wide definition, which can be derived from molecular, histologic, radiographic, and physiological aspects, includes therapeutic approaches. (1) Using biomarkers in clinical settings -Clinical biomarkers are easier and less expensive to use than direct measurement of the ultimate clinical goal, and they are usually measured over a shorter time period. Pharmacodynamics and dose-response studies, cell type identification, prognostic markers, tailored therapeutic interventions, sickness screening, diagnosis, characterisation, and monitoring, and the prediction and treatment of adverse drug responses are some of their uses.(2)
Cancer, diabetes, and kidney stone disease represent major global health challenges, each characterized by distinct yet interrelated biological alterations that can be detected through specific biomarkers. In cancer, biomarkers enable early detection, prognosis assessment, and monitoring of therapeutic response by reflecting genetic, proteomic, and metabolic changes associated with tumor development. Diabetes relies heavily on metabolic and inflammatory biomarkers that reveal disruptions in glucose regulation and systemic complications. Meanwhile, kidney stone disease involves biochemical markers that indicate abnormalities in mineral metabolism and renal function. Together, these biomarker categories provide critical insights into disease mechanisms and offer powerful tools for improving diagnosis, treatment, and personalized patient care.

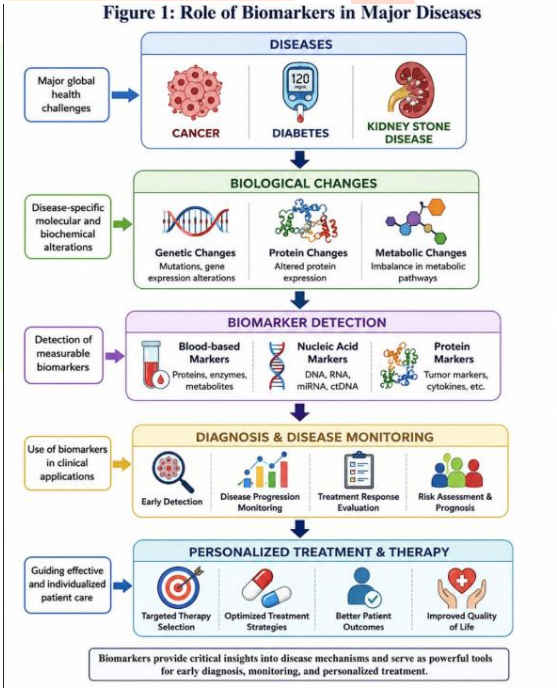

Figure No.1: Schematic representation showing the role of biomarkers in diagnosis, monitoring, and personalized treatment of major diseases.

Biomarkers In Cancer :-

Biomarkers are the amounts or activities (the capacity of genes or proteins to carry out their roles) of a range of genes, proteins, or other biological traits. features that are unique to each kind of cell As a result, biomarkers provide an impartial means of evaluating or assessing normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention. Gene rearrangements, point mutations, and gene amplifications are among the many genetic changes Therefore, biomarkers

offer an objective way to evaluate or analyse pathogenic processes, normal biological processes, or pharmacological reactions to a treatment intervention. In addition to being predictive, These changes can be used as biomarkers to find and create tailored treatments.

when they appear in most people with a certain kind of cancer Reactions to different therapies (3)

Need of Cancer Biomarkers :-

Historically, 2D separations of gels or

the identification of Cancer-related immunogenic antigens

have been used to find cancer protein biomarkers in bodily fluids and tumour tissues (or cell lines). The cell Thus far, traditional methods have yielded nine blood-based cancer biomarkers that have received FDA approval, the majority of which are employed for treatment monitoring. Over the past ten years, The quantity of novel proteins biomarkers that receive FDA approval has declined to the threshold at which only 0–3 new markers are authorised per year (across all Disorders) . Given this disheartening downward tendency, it appears that traditional methods have done what they could and that new methods and cutting-edge technologies to find new protein biomarkers with potential use in medicine. (4) We have significantly decreased the illness load thanks to early detection methods like colonoscopies and pap smears. Carcinoembryonic antigen (CEA), cancer antigen 125 (CA125), prostate-specific antigen (PSA), and alpha-fetoprotein (AFP) were among the few early detection markers that were very non-specific and inaccurate. The scientific community as a whole used high-throughput screening systems to find biomarkers because of the shortcomings in finding reliable biomarkers. (5)

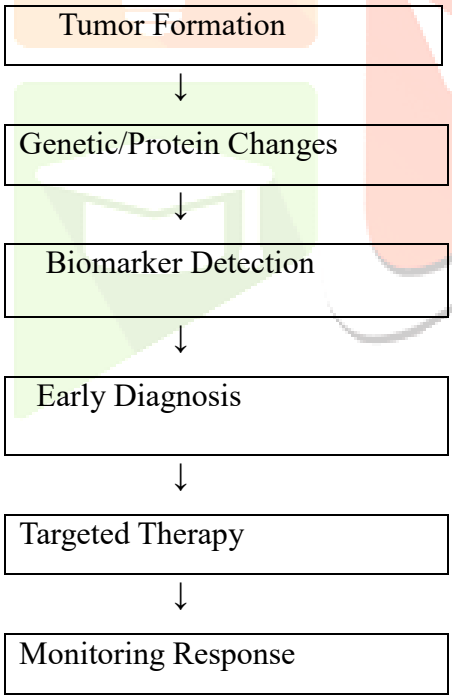

Figure No:2- Application of Cancer Biomarkers

Various Biomarkers In Cancer :-

Circular RNA is a new kind of biomarker in cancer

One new kind of cancer biomarker is circular RNA. Circular RNA's role as a cancer biomarker: By influencing the level of expression of genes at the transcriptional or CircRNAs can serve as mi at the post-transcriptional stage. miRNA sponges, regulators of gene transcription and expression, RBP

sponges, and protein/peptide translators. (6) CircRNAs may be crucial to the onset and progression of cancer, according to recent research. CircRNAs might serve as biomarkers for certain malignancies to aid in diagnosis. CircRNAs may be molecular indicators of tumours, as recent research has partially demonstrated. CircRNAs in gastric cancer: (GC) In GC tissues, Circ-PVT1 is over expressed .Through the amplification of its genetic locus and might .Function A sponge against members of the miR-125 family to promote GC cell proliferation. Hsa_circ_0000190 was recently discovered to be a possible Biomarker for the diagnosis of stomach cancer . Both GC tissues and GC patient plasma showed down-regulation of it. hsa_circ_0000l190 exhibits superior sensitivity and specificity when compared to two traditional biomarkers for GC, CEA (carcinoembryonic antigen) and CA19-9. (7).

Table No :1- Important Biomarkers Used in Cancer Diagnosis and Prognosis

Biomarker	**Function**	**Clinical Use**
Circular RNA	Gene regulation	Cancer diagnosis
Survivin	Inhibits apoptosis	Prognosis
ctDNA	Tumor DNA detection	Tumor monitoring
Exosomes	Cell communication	Early detection
Protein biomarkers	Protein expression	Cancer typing

A molecular biomarker for cancer, such as survivin:

Apoptosis protein is inhibited by survivin, which is produced in many cancers. Poorer clinical outcomes and more aggressive illness are correlated with its expression levels. Because survivin expression is low in healthy tissues, it has emerged as a prime target for anti-cancer treatments as well as tumour diagnostic and prognostic applications. (8) Any quantifiable A molecular cancer biomarker is a molecular predictor of cancer risk, cancer occurrence, or patient outcome. Examples include germline or somatic genetic variants, proteomic signatures, transcriptional changes, and epigenetic signatures. These indicators are based on biomolecules, such as proteins and nucleic acids. It is present in samples obtained from tissues using tumour biopsies or, in a more straightforward and non-intrusive way, manner, from saliva, buccal swabs, blood (or serum or plasma), stool, urine, etc. Nanotechnology, next-generation sequencing, and methods for analysing circulating cancer DNA/RNA or exosomes are only a few of the detection technologies that have advanced significantly over the last few decades.(9)

Cancer protein biomarker:

Clinical outcomes may be enhanced by protein biomarkers that enable early diagnosis of primary HNSCC or relapse. Although it is currently challenging, screening for precursor alterations in the mucosal linings that occur before invasive tumours emerge and for precise risk prediction of malignant transformation may present advantageous chances. (10).For effective treatment, it is essential to accurately identify the histological type of cancer and the corresponding protein biomarkers. Without understanding the nature and origin of malignant cells, which release specific protein biomarkers into the bloodstream, identification of lung cancer is impossible due to the wide variation in molecular-biological characteristics of its histological forms. Various biomarker panels are currently employed for screening. (11).

A tumour that circulates One new kind of cancer biomarker is DNA: -Genomic data pertaining to tumours, including methylation, microsatellite instability, mutation, and other traits, can be found in ctDNA, a little DNA fragment extracted from tumour cells. It is the perfect biomarker for tracking the growth of tumours in real time. The various ctDNA sources , including urine and blood , ascites, cerebrospinal fluid, etc, are mostly reviewed in this book. Through tumour. apoptosis, circulating exosome secretion, cell necrosis, etc., The circulatory system may be traversed by ctDNA. And convey the hallmark alterations of tumours, including methylation, mutation, microsatellite instability, gene rearrangement, etc. A number of In order to describe the preparation procedure before ctDNA analysis and the detection methods of two gene-level changes, this paper combines new materials with enrichment detection techniques derived from PCR, sequencing-based detection techniques, and comprehensive detection techniques. ctDNA mutation and methylation. Additionally, a summary of the function of ctDNA in early It offers early screening, diagnosis, molecular typing, prognosis prediction, monitoring for recurrence, and therapeutic recommendations.(12)

Exosomes may be a biomarker: -

Most live cells emit Nano vesicles called exosomes, which have a diameter of 50–100 nm. Exosome proteins and RNA are examples of exosome-associated diagnostic molecules. Finding comparatively low-expression biomarkers that would otherwise go unnoticed is made easier by the , the exosomal source's enrichment of diagnostic markers, which results from exosome sorting of cargo.(13).

Need of Diabetis Biomarkers :-

The need for reliable diabetes biomarkers has grown increasingly important as the global burden of diabetes continues to rise and early metabolic disturbances often go undetected until significant complications develop. Traditional diagnostic tools, such as fasting glucose and HbA1c, provide valuable but limited information, underscoring the demand for more sensitive and specific biomarkers capable of identifying individuals at risk before overt hyperglycaemia occurs. Advanced biomarkers can offer deeper insights into pancreatic β-cell function, insulin resistance, inflammation, and oxidative stress, thereby enabling earlier diagnosis, improved disease stratification, and more precise monitoring of therapeutic responses. Moreover, comprehensive biomarker panels hold significant potential for predicting long-term complications and guiding individualised treatment plans, which eventually enhance patient outcomes and lower HealthCare burdens. 46.5% of the approximately 410 million diabetic people worldwide are undiagnosed, according to the International Diabetes Federation's (IDF) Diabetes Atlas (Seventh Edition, 2015). The quantity of those who have diabetes could reach 642 a million by 2040. (14) An absolute or relative shortage of insulin, along with hyperglycaemia, dyslipidaemia, and neurovascular damage, are the hallmarks of diabetes mellitus, a chronic illness that is becoming more and more common. Every organ system in the patient's body may be impacted, which could lower their quality of life and burden the local and international economies and communities. (15).

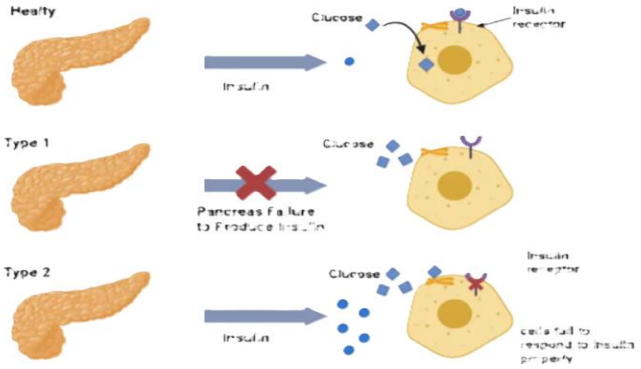

Figure No.3: Diabetes Biomarker Pathway

Various Biomarkers Of Diabetis:-

Serum biomarker:

Numerous factors, such as genetics and environmental triggers and moderators, contribute to the development of T1D. None of these elements, nonetheless, can be used as a precise diagnostic standard. In addition to various T1D-specific biomarkers that differentiate T1D from other subtypes of diabetes, the current diagnostic biomarkers of T1D still depend on the effects of hyperglycaemia, such as the consequent elevated glucose or glycated haemoglobin. (16)

Cardiac biomarker in type 2 diabetes: -

Research indicates that traditional cardiovascular risk factors negatively impact the mortality and standard of living of individuals with type 2 diabetes. It is proposed that biomarkers for heart that represent different stages of cardiac pathophysiology remodelling, including Extracellular matrix, fibrosis, hypertrophy, inflammation, necrosis/apoptosis, and biomechanical stress remodelling, would have a significant added value for predicting clinical results (death, MACEs, hospitalisation, and HF onset) in the group of patients Furthermore, measuring the levels of cardiac biomarkers in the blood can reveal novel individual prognostic data that may have significant predictive ability in addition to Conventional cardiovascular risk factors But each the price, superiority, predictive value, sensitivity, specificity, and face-to-face comparison. We paper on heart biomarkers whose prognosis value has been proven and are still being investigated because to the numerous circulating biomarkers with dubious ability to forecast clinical outcomes in individuals with DM and pre-DM. (17)

HbA1c biomarker:-

This biomarker, which shows how lifestyle choices and medication have affected glycaemic control over the last three months, is helpful in the diagnosis, prevention, and monitoring of diabetes mellitus. Furthermore, those with pre-diabetes who have HbA1c levels between 5.7% and 6.4% are more likely to acquire diabetes mellitus. Diabetes consequences decrease after strict glycaemic management and decreased HbA1c levels; at HbA1c <7%,The incidence of diabetic retinopathy, diabetic nephropathy, peripheral neuropathy, and cardiovascular disease risk has decreased by 76%, 54%, and 35%, respectively. . However, among Individuals with both type 1 and type 2 diabetes lowering HbA1c levels is linked to an increased risk of hypoglycaemia prevalence. Numerous studies have shown that hypoglycaemia in diabetes patients is negatively correlated with HbA1c. (18)

Circular microRNA:-

The part miRNAs play in the aetiology of diabetes A distinct group of miRNAs is expressed by insulin target tissues and pancreatic β-cells. The majority of them are broadly dispersed throughout human tissues and are not cell-specific. One prominent exception is miR-375, a miRNA that controls gene expression and is substantially enriched in pancreatic islets. engaged within the β-cell mass expansion in reaction to insulin resistance and hormone secretion (19) It was discovered that miR-375, one of these non-coding RNAs, is crucial to β-cell function. In fact, by regulating myotrophin levels, miR-375 adversely affects glucose-stimulated insulin production . The precise function of this protein in the β-cell secretory process is yet unknown, although RNA interference mirrored the effect of miR-375 on insulin production by reducing myotrophin expression. (20)

Glycated albumin:-

The GA decrease is around ten times higher than the HbA1C. GA is a better measure of glycaemic control than HbA1C when glycaemic control changes quickly as a result of beginning or stopping diabetes medication. However, when the short-term glycaemic control status deteriorates, GA rises before HbA1C. Consequently, GA makes it possible to identify the deterioration of glycaemic control earlier in such circumstances. It is well recognised that when fulminant type 1 diabetes mellitus is diagnosed, the HbA1C remains normal or only slightly increased. This condition causes the pancreatic β cells to be rapidly destroyed, which raises plasma glucose and causes ketoacidosis in the near term. (21)

Table No.2: Major Biomarkers Used in Diabetes Diagnosis and Monitoring

Biomarker	**Role**	**Clinical Importance**
HbA1c	Long-term glucose control	Diabetes diagnosis
Serum biomarkers	Detect metabolic changes	Early detection
Cardiac biomarkers	Cardiovascular risk	Prognosis
miRNA	β-cell regulation	Disease mechanism
Glycated Albumin	Short-term glucose monitoring	Therapy assessment

Need of Kidney Stone Biomarkers The need for reliable kidney stone biomarkers has become increasingly critical as the incidence and recurrence of nephrolithiasis continue to rise worldwide. Current diagnostic methods, such as imaging and basic urine chemistry, offer limited insight into the underlying metabolic disturbances that drive stone formation. Sensitive and specific biomarkers are essential for identifying individuals at high risk, detecting early biochemical alterations, and distinguishing between different stone types and etiologist. Such biomarkers can improve the prediction of recurrence, guide personalized dietary and pharmacological interventions, and provide a non-invasive means of monitoring treatment efficacy. Ultimately, the development and validation of robust kidney stone biomarkers have the potential to enhance early prevention strategies, reduce the need for repeated imaging, and significantly improve long-term patient management.

Nephrolithiasis, which refers to stones that develop in the renal calyx, renal pelvis, and the junction of the renal pelvis and ureter, is one of the most prevalent urinary illnesses and is becoming more commonplace globally. When the solubility and precipitation of salts that form stones in the kidney and urinary tract are balanced, nephrolithiasis results (22). Unlike a risk factor or susceptibility, like albuminuria, a biomarker can be used as a surrogate endpoint to increase the effectiveness of clinical trials and reduce the requirement for a lengthybility marker. A biomarker is a dynamic indicator of the activity of biologic research of diseases that proceed slowly. It has a trajectory and tempo. In addition to their usage in clinical trials (for drugs that exist), a risk factor may irrespective of whether renal screening, patient selection, or surrogate outcomes are present (23)

Various Biomarkers In Kidney Stone :-

Calcium oxalate monohydrate binding protein:

In contrast to COM crystals, CaOx dihydrate (COD) is more frequently observed in asymptomatic crystalluria. More frequently discovered in stone formers' urine.By decreasing adhesion to renal tubule cells, the production of COD rather than COM may offer protection against stone disease . Conversely, compared to a comparable calcium load, an The likelihood of stone formation is almost tripled by an oxalate load. Therefore, the difficulty of identifying and differentiating differentiating between stone formers and non-stone formers can be resolved by identifying macromolecules that are modulators. A 45 kDa COM binding protein that we have identified encourages CA Ox crystallisation . It is made up of fundamental amino acids and can be detected in the proximal and distal tubules of the kidney. It is discovered to exist in the mitochondria and nucleus at the subcellular level (data not shown). Our goal in this study was to determine if this Protein may serve as a diagnostic sign for individuals predisposed to calcium oxalate kidney stones. the purpose of identifying the illnesses' beginning or recurrent presence. (24)

Table No.3: Comparative Overview of Biomarkers-

Disease	Major Biomarkers	Main Application
Cancer	ctDNA, Exosomes, Survivin	Early diagnosis
Diabetes	HbA1c, miRNA, GA	Glucose monitoring
Kidney Stone	COM binding protein	Stone prediction

Discussion: -

The power of biomarkers to enhance illness diagnosis, prognosis, and therapy monitoring has made them extremely important in contemporary healthcare. The clinical significance of biomarkers in kidney stone disease, diabetes, and cancer—some of the most prevalent illnesses in the world—is highlighted in this review. Personalized medicine and early intervention techniques are supported by many biomarkers that offer useful information about illness development, molecular changes, and therapy response.Circular RNAs, survivin, circulating tumor DNA (ctDNA), exosomes, and protein biomarkers are examples of cancer biomarkers that have demonstrated promise uses in targeted therapy and early diagnosis. These biomarkers may enhance treatment decision-making by identifying genetic and molecular alterations linked to tumor growth.

The sensitivity and specificity of cancer biomarker detection have been considerably improved by recent developments in molecular biology and sequencing technologies. Glucose monitoring and problem prediction are greatly aided by diabetes biomarkers, such as HbA1c, glycated albumin, serum biomarkers, cardiac biomarkers, and microRNAs. These biomarkers shed light on β-cell malfunction, insulin resistance, and cardiovascular risks related to diabetes mellitus. Advanced biomarkers may help identify diabetic problems earlier and treat them more successfully.Similar to this, metabolic markers and kidney stone biomarkers such calcium oxalate monohydrate binding proteins are helpful in

identifying those who are at a high risk of developing nephrolithiasis and having it reoccur. These biomarkers have the potential to enhance kidney stone disease preventative tactics and direct individualized treatment plans.Despite the enormous therapeutic potential of biomarkers, problems including poor standardization, high cost, and the requirement for extensive validation studies still exist.

Future Perspectives of Biomarkers:-

Future biomarker development is anticipated to improve precision medicine in cancer, diabetes, and kidney stone disease by enabling individualized treatment strategies based on a patient's molecular profile. Advanced biomarker panels may help clinicians predict disease progression, evaluate treatment response, and reduce complications through continuous monitoring. The field of biomarker research is rapidly advancing with the integration of modern technologies such as artificial intelligence, genomics, proteomics, and nanotechnology. These developments are assisting scientists in finding extremely specific and sensitive biomarkers that can identify illnesses in their early stages. Because they offer safer, quicker, and more practical ways to diagnose and track diseases, non-invasive diagnostic techniques utilizing blood, urine, saliva, and other bodily fluids are becoming more and significant.Future biomarker development is anticipated to enhance precision medicine in kidney stone disease, diabetes, and cancer by providing customized treatment plans based on a patient's molecular profile. Through ongoing monitoring, advanced biomarker panels may assist medical professionals in forecasting the course of a disease, assessing the effectiveness of a treatment, and minimizing complications. Technologies like microRNA profiling, circulating tumor DNA analysis, and biosensor-based detection systems are demonstrating encouraging outcomes for clinical real-time applications. Additionally, the integration of digital healthcare systems with biomarker science may greatly enhance patient care and save healthcare expenses. Large biomarker datasets can be analyzed with the use of artificial intelligence and machine learning to provide precise diagnosis and prognosis. It is anticipated that in the future, biomarker-guided medicines and personalized healthcare techniques would improve quality of life, improve treatment outcomes, and aid in the creation of more potent preventive measures in contemporary medicine.

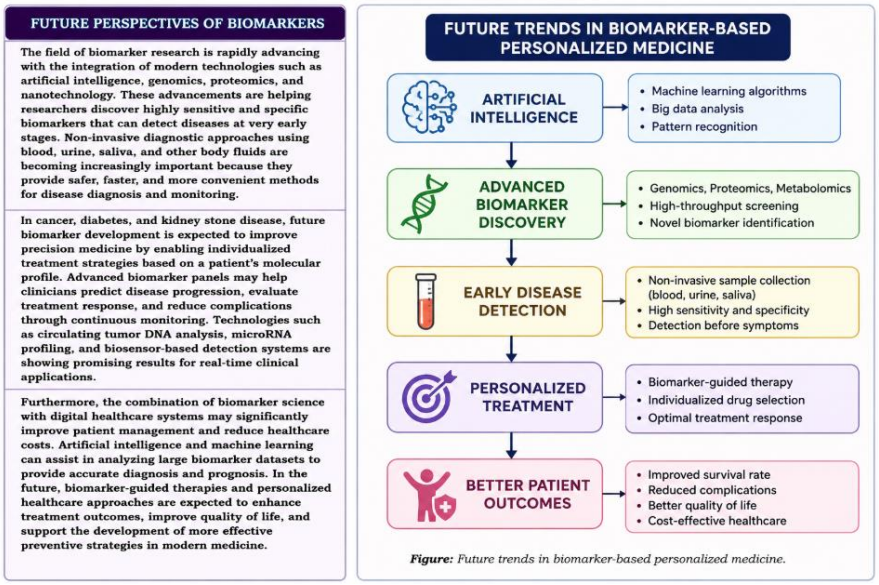

Figure 4: Future trends in biomarker-based personalized medicine.

Conclusion:-

In order to diagnose, track, and treat serious illnesses including cancer, diabetes, and kidney stone issues, biomarkers have become indispensable tools. They help doctors make quicker and more precise judgements by offering important information on the start, course, and response to therapy of diseases. While diabetes biomarkers enhance glucose monitoring and forecast long-term consequences, cancer biomarkers aid in the early detection of tumours and direct tailored therapy. Biomarkers for kidney stones help detect metabolic risks and stop recurrence. In general, the application of biomarkers improves patient outcomes, individualised treatment, and early detection. Their clinical utility in contemporary medicine will increase with more investigation.

Acknowledgement:-

he authors express sincere gratitude to their respected teachers, mentors, and institution for their continuous guidance, encouragement, and support during the preparation of this review article. The authors also acknowledge all researchers and scientists whose published studies and valuable contributions formed the scientific basis of this paper. Finally, the authors are thankful to everyone who directly or indirectly contributed to the successful completion of this work.

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